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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/608,463	06/27/2003	James W. Ryan	JR-10,003-US	6428
25538	7590	05/14/2008		
CHERYL H AGRIS PHD PO BOX 806 PELHAM, NY 10803			EXAMINER SLOBODYANSKY, ELIZABETH	
			ART UNIT 1652	PAPER NUMBER
			MAIL DATE 05/14/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/608,463	Applicant(s) RYAN, JAMES W.	
	Examiner Elizabeth Slobodyansky, PhD	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7, 10, 12, 14-18, 20, 22-25 and 30-38 is/are pending in the application.
- 4a) Of the above claim(s) 12, 14, 22, 23 and 32-38 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7, 10, 15-18, 20, 24, 25, 30 and 31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/3/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

In view of the Supplemental Appeal Brief filed on March 2, 2008,
PROSECUTION IS HEREBY REOPENED. A new ground of rejection is set forth
below.

To avoid abandonment of the application, appellant must exercise one of the
following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply
under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed
by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and
appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth
in 37 CFR 41.20 have been increased since they were previously paid, then appellant
must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by
signing below:

/Nashaat T. Nashed/
Supervisory Patent Examiner
Art Unit 1652.

Claims 7, 10, 12, 14-18, 20, 22-25 and 30-38 are pending. Claims 12, 14, 22, 23
and 32 have been previously withdrawn.

Claims 7, 10, 15-18, 20, 24, 25, 30 and 31 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 10, 15-18, 20, 24, 25, 30 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 7, with dependent claims 10, 15-18, 20, 30 and 31, has been amended on March 3, 2005 and August 29, 2005 and claim 24, with dependent claim 25, was added on March 3, 2005 and amended on August 29, 2005 to recite "wherein a sequence segment comprising 41738-9502 of SEQ ID NO:4 encodes human mouse double minute 2 homolog depicted in SEQ ID NO:2, ... a region comprising a dinucleotide of the following group: 41739-41738, ...". Applicant does not indicate and the examiner is unable to locate adequate support in the specification for such positions in SEQ ID NO:4, *i.e.* 41738-9502 and 41739-41738. Thus there is no indication that the specific segment of 41738-9502 of SEQ ID NO:4, *i.e.* said specific positions in SEQ ID NO:4 were within the scope of the invention as conceived by Applicants at the time the application was filed.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 7, 10, 15-18, 20, 24, 25, 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muzny et al. in view of Vogelstein et al.

Muzny et al. (150579 bp, GenBank accession AC025423, March 9, 2000, cited on form PTO-892 mailed 12/1/04) teach the sequence of human chromosome 12 comprising the sequence of SEQ ID NO:4 (51039 bp) of the instant invention.

Vogelstein et al. (US Patent 5,411,860, GenBank accession NM_002392, cited on form PTO-892 mailed 12/1/04) teach cloning, functional expression and chromosomal localization of human mouse double minute (MDM2) homolog. They teach cDNA (SEQ ID NO:1) encoding human MDM2 homolog (SEQ ID NO:2, 491 amino acids) that is 100% identical to the human MDM2 homolog of the instant invention (SEQ ID NO:2). Using a labeled probe, they localized the gene encoding said human MDM2 homolog to chromosome 12q12-14 (column 5, lines 2-13; the description of SEQ ID NO:1 in the Sequence Listing). Vogelstein et al. teach that human MDM2 binds to oncogene p53 and is diagnostic of tumorigenesis (e.g., column 3, lines 20-35). SEQ ID NO:1 taught by Vogelstein et al. comprises 5' non-coding region consisting of nucleotides 1-311. The elected species of 41739-41738 correspond to exon-intron junction within the genomic DNA corresponding to said 5' non-coding region.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use said cDNA taught by Vogelstein et al. to identify the genomic DNA that encodes the human MDM2 homolog of SEQ ID NO:2 on chromosome 12. The motivation is provided by Vogelstein et al. who teach that it binds to oncogene p53 and is diagnostic of tumorigenesis (e.g., column 3, lines 20-35). The state of the art provides various techniques for obtaining genomic DNA using cDNA probes that are usually labeled. The comparison of genomic and cDNA would result in the identification of regions comprising exon-intron and intron-exon junctions within coding and non-coding regions. One of ordinary skill in the art would have been motivated to use said non-coding regions or fragments thereof of at least 20 nucleotides and up to 5000 or 51039 nucleotides (the entire length of SEQ ID NO:4) nucleotides for detecting splice variants of the genomic DNA encoding human MDM2 homolog in genomic nucleotide samples from an individual, for example. As a matter of convenience a non-coding region such as an exon-intron or intron-exon region or fragments thereof can be present in a kit or on a solid support. Further, said support can be a microarray according to a customary use of nucleic acid molecules in the art.

Response to Arguments

Applicant's arguments filed March 2, 2008 have been fully considered but they are not persuasive.

With regard to the 103(a) rejection, Applicant's arguments can be summarized as follows: 1) Muzny contains a small portion of chromosome 12, where the location of the

MDM2 gene was indicated by Vogelstein as 12q12-14 while Applicant found it on 12q and 2) the MDM cDNA constitutes only 1.6% of the clone disclosed by Muzny, therefore it would be undue experimentation to locate the MDM2 gene and identify its exon-intron junctions.

Applicant argues "In Appellant's view, it would not have been obvious to combine the disclosure of Muzny and Vogelstein given that there was no suggestion to do so. Muzny merely contains just a small portion of chromosome 12 DNA. Chromosome 12 is about 130 million base pairs long and is believed to contain several hundred genes (by analysis after 2001 and after the Applicant discovered the human MDM2 homologue gene). Muzny et al knew that clone AC025423 (from 1VII-61102) was from chromosome 12 but there is no evidence in the NCBI report of a sub-assignment to the p- or q-arm. Further, there is no evidence that Muzny knew whether the clone did or did not contain one or more genes and particularly whether it contained the gene encoded by SEQ ID NO:4. As will be discussed in further detail below, the MDM2 cDNA constitutes just 1.6% of the clone disclosed by Muzny. Undue experimentation would have been required not only to locate the MDM2 gene but also identify exon-intron junctions" (Supplemental Appeal Brief of 3/2/08, page 11).

Applicant further argues Second, Appellant asserts that there would not be a reasonable expectation of success of obtaining the claimed noncoding sequences of SEQ ID NO:4 in view of the cited references. Vogelstein placed the human MDM2 homologue gene at 12q12-14. As noted above, there was actually a previous disclosure stating that the MDM2 was located between 12q14.3-15 (see, for example, Andersen et

al., 1996, Mammalian Genome 7:780-783 and Bureau, 1995, Genomics 28: 109-112, submitted and disclosed in previous response attached hereto as Exhibit 1). However, given the conflicting locations published as of the priority, one of ordinary skill in the art would not have known which location was actually correct" (Brief, page 14).

This is not agreed with because the actual location does not matter as long as it is a part of the Muzny sequence, which it is. Applicant did not need to separate the Muzny sequence into the fragments containing different arms of chromosome 12. In fact, Applicant did not isolate the fragment 12q12-14 or 12q14.3-15. He run cDNA against the genomic DNA disclosed by Muzny and found the location of the gene where it was. This experiment was performed according to the knowledge and the state of the art as evidenced by Watson et al. Watson et al teach that "once the first genes were cloned, introns were identified by comparing the cloned genomic DNA with the corresponding cloned cDNA" ("Recombinant DNA", page 137, 2nd column, form PTO-892 mailed 4/16/07). Applicant's argument would be convincing if the exact location would need to be known before the comparison of the genomic and the cDNA is made. This is not the case because the work is done on the genomic DNA that is known without fragmentation thereof. Applicants further argues that "Watson would not apply in this case since in Watson, the genes themselves were actually cloned" (ibid, page 18, last sentence). Thos is not persuasive because Muzny provided the piece of the genomic DNA containing the requisite gene. Having the cDNA, it does not require undue experimentation to identify the fragment of the genomic DNA corresponding to the gene and exon-intron locations within said gene.

The second type of Applicant's arguments concerns with the fact that the cDNA constitutes only 1.6% of the genomic DNA. While the large quantity of the experimentation may be involved, it is not undue because the sufficient guidance and knowledge are provided by the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed, PhD can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Elizabeth Slobodyansky/

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

May 12, 2008